Remarks

No claim amendments are made in this paper, and thus claims 7-12, 21-28, 32-39, 43-44 and 47-54 are pending in this application. No new matter has been introduced. Applicant respectfully submits that the pending claims are allowable for at least the following reasons.

A. The Rejection under 35 U.S.C. § 112 Should be Withdrawn

a. Enablement

In item 14 of the Office Action, the rejection of claims 7-12, 21-28, 32-39, 43-44, and 47-48 as allegedly not enabled is maintained. Office Action, page 9. In particular, the Examiner maintains his allegation that while the specification enables the treatment of diseases of corneal neovascularization and Crohn's disease, and V2-carcinoma, it does not provide enablement for "inhibiting angiogenesis" and "treating angiogenesis dependent disease." Office Action, page 9. Applicant respectfully traverses this rejection.

First, Applicant respectfully submits that the pending claims are enabled because the specification "contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented." *Manual of Patent Examining Procedure* ("MPEP"), § 2164.04. Further, Applicant respectfully submits that no undue experimentation is necessary for the reasons submitted in his previous response. *See* Applicant's Response of February 22, 2005, pages 21-22.

In response, the Examiner dismisses Applicant's argument based on his conclusory statement that "the specification is only enabled for the angiogenesis inhibiting compound ... and supidimide and only for the treatment of the diseases of corneal neovascularization and Crohn's disease, and V-2 carcinoma." Office Action, pages 3, items 5 (emphasis in original). However, no explanation or reasoning as to why the Examiner regards the specification to be enabling only for such subject matter is not provided. Applicant respectfully points out that such a conclusory statement, without any basis or reasoning, is insufficient to overcome the presumption that the claims are enabled. *See, e.g., In re Wright*, 999 F.2d 1557, 1562 (Fed. Cir. 1993) (holding that the burden to initially establish a reasonable basis to question the enablement is on the examiner).

Further, the Examiner alleges that no sufficient guidance is provided by the specification. Office Action, page 4, item 6. In particular, the Examiner alleges that there is "no clear guidance and direction to enable the skilled artisan to make and use every functional compound of ... claim 7 that is further combined with [the compounds encompassed by] the functional recitation of anti-inflammatory drug[1] ... and .. to treat [the ailments encompassed by] the broad functional recitation of 'angiogenesis dependent disease'." *Id.* (emphasis added). Applicant respectfully disagrees with the Examiner's assessment of the pending claims.

First, the Examiner is essentially requiring that the specification disclose the pharmacological activity of "every functional compound" encompassed by the genus recited by the pending claims. However, Applicant respectfully points out that such a requirement is contrary to the well-established principles regarding enablement. This is because, "[f]or a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient," and "[p]roof of enablement will be required for other members of the claimed genus only where adequate reasons are advanced by the examiner." MPEP, § 2164.02. As the Examiner appears to recognize, the specification provides representative examples of the claimed genus. Further, the Examiner does not provide any specific reasons as to why the enablement for other compounds in the claimed genus is doubted.

The Examiner further appears to imply that because the specification discloses, as examples, the treatment of certain exemplary diseases using certain exemplary compounds of the invention, the invention is limited to the treatment of the specific diseases using the specific compounds disclosed as examples. However, such a proposition is flatly contrary to the well-established legal principles. This is because "compliance with the enablement requirement does not turn on whether an example is disclosed," since "[t]he mere fact that something has not previously been done clearly is not, in itself, a sufficient basis for rejecting all applications purporting to disclose how to do it." MPEP § 2164.02 (citing *Gould*

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[1] Applicants respectfully submit that the term "anti-inflammatory drug" is also enabled by the specification and the ordinary skill in the art because the term is widely used and accepted in the art. Consequently, those of ordinary skill in the art would have been able to make and use the "anti-inflammatory drug" without undue experimentation.

v. Quigg, 822 F.2d 1074, 1078 (Fed. Cir. 1987)).[2] As the specification provides adequate representative compounds and their use for the representative disorders, Applicant respectfully submits that the pending claims are enabled.

Furthermore, contrary to the Examiner's allegation, no undue experimentation is necessary to practice the claimed invention. *See* Office Action, page 4, item 7. In reaching the conclusion that undue experimentation is necessary, the Examiner again appears to rely on the conclusory proposition that the specification only enables what is disclosed as examples. As discussed above, however, that proposition is legally unfounded, and the Examiner does not provide any reasoning or evidence to the contrary. Therefore, to the extent that the Examiner's contention that undue experimentation is required is based on a conclusory statement without any reasoning or evidence, Applicant respectfully submits that the rejection of the pending claims should be withdrawn.

For at least the foregoing reasons, Applicant respectfully submits that the pending claims are enabled, and thus, requests that the rejection thereof be withdrawn.

b. Written Description

In item 15 of the Office Action, claims 27, 28, 37-39, and 48 are rejected for allegedly failing to comply with the written description requirement. In particular, the Examiner alleges that those of ordinary skill in the art, reading the specification, would not have concluded that the inventor had possession of the claimed invention because "the definitions of angiogenic [sic] dependent diseases or angiogenic [sic] associated diseases are not definitive." Office Action, page 5, item 8. However, Applicant again respectfully invites the Examiner's attention to page 1, line 30 - page 6, line 14 of the specification. As the Examiner will see, this portion of the specification provides a clear definition of the term "angiogenesis," and sets forth the types and examples of diseases associated with angiogenesis. Consequently, Applicant submits that the definitions of angiogenesis dependent or associated diseases are clearly provided in the specification, and those of ordinary skill in the art would have understood what types of diseases are encompassed by these terms.[3] Therefore, Applicant respectfully requests that the rejection of the pending claims under 35 U.S.C. § 112 be withdrawn.

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[2] Indeed, the specification does disclose sufficient examples for those of ordinary skill in the art to understand that Applicant had a possession of the claimed invention.

[3] Despite this apparent fact, the Examiner dismisses what the specification discloses as "not definitive," and alleges that the specification does "not provide the artisan with precise definitions and

B. The Rejection of Claims 7-12, 21-28, 32-39, 43-44, and 47-48 Under 35 U.S.C. § 103(a) Should Be Withdrawn

In items 18-20 of the Office Action, the rejection of the pending claims as allegedly obvious over WO 95/03807 by Billson *et al.* ("Billson"), optionally in combination with U.S. Patent No. 5,348, 942 to Little, II *et al.* ("Little"), is maintained. In particular, it is alleged that the claims are obvious because: 1) Billson "clearly and specifically teach[es] of administering thalidomide and a steroid ... as do the instant claims"; 2) "it is surely within the level of skilled artisan to utilize derivatives and analogues of a compound such as thalidomide as long as the inherent properties of a given compound ... are not materially changed"; 3) the claimed compounds, through cyclization, form thalidomide, and such "internal cyclization reactions are obvious to one having ordinary skill in the art"; and 4) a clear motivation to make a composition that comprises thalidomide and a steroid is provided by Billson. Office Action, items 9-12. Applicant respectfully disagree with each of these allegations.

First, Applicant respectfully points out that the assertion that the instant claims are "clearly and specifically" taught by Billson is factually incorrect. As the Examiner states, Billson purportedly discloses the administration of thalidomide and a steroid. In contrast, claim 7, the broadest composition claim, recites a genus of angiogenesis inhibitory compounds, which does not encompass thalidomide. Therefore, to the extent that the rejection is based on this incorrect understanding of facts, Applicant respectfully requests that the rejection be withdrawn.

Second, the Examiner's contention that the pending claims are obvious because "it is surely within the level of skilled artisan to utilize derivatives and analogues of a compound such as thalidomide as long as the inherent properties of a given compound ... are not materially changed" is legally unfounded. Apparently, the Examiner is suggesting that the pending claims are obvious because those of ordinary skill in the art could have made any number of derivatives and analogues to arrive at the claimed invention. However, as well-settled, a *prima facie* case of obviousness requires that the prior art references themselves must provide the motivation to combine or modify. *See Noelle*, 355 F.3d 1343, 1352 (Fed. Cir. 2004) ("the suggestion ... 'must be founded in the prior art, not in the applicant's disclosure.'" (quoting *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991)). Accordingly, the

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meanings." However, the Examiner fails to provide any explanation as to why the specification does not provide such information. Such a conclusory statement, without any reasoning or evidence, simply begs the question.

question is whether those of ordinary skill in the art, form the disclosure of the prior art references, would have been motivated to make and use the claimed invention, not whether such persons could have made the claimed invention. *See In re Mills*, 916 F.2d 680, 682 (Fed. Cir. 1990) (holding that the mere fact that prior art references can be combined or modified does not render the combination obvious unless the prior art also suggests the desirability of the combination).

The Examiner also appears to suggest that the pending claims are obvious because those of ordinary skill in the art could have tried numerous derivatives and analogues until they find the compounds that possess the similar properties as those disclosed in Billson. Such an analysis is also flatly contrary to the well-settled legal principle that whether or not something may have been "obvious to try" cannot form the basis for a proper obviousness rejection. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1380 (Fed. Cir. 1986) (citing *Jones v. Hardy*, 727 F.2d 1524, 1530 (Fed. Cir. 1984) ("obvious to try" is improper consideration in adjudicating obviousness issue)). Consequently, Applicant respectfully submits that the Examiner's analysis is legally flawed, and thus, submits that the rejection of the pending claims should be withdrawn.

Finally, the Examiner appears to contend that, when the angiogenesis inhibitory composition is represented by the Applicant's compounds P, Q, R or S in claim 9, one of skill in the art would recognize that these compounds would easily produce thalidomide via an internal cyclization reaction. However, the cyclic imide formation allegedly disclosed in Solomons (provided by the Examiner) involves a primary amine, while one of the hydrogens in amine groups present in compounds P, Q, R, and S is replaced with a bulky chemical moiety. As such, those of ordinary skill in the art would have concluded that the presence of such a bulky chemical moiety would sterically hinder the formation of cyclic imide, as opposed to the unsubstituted primary amine group purportedly disclosed in Solomons. Furthermore, Solomons purportedly discloses that the formation of cyclic imide occurs at an elevated temperature, with the required heating of the reaction to 150-160°C. Solomons, page 802. As such, even apart from the steric hindrance, those of ordinary skill in the art could not have believed that compounds P, Q, R, and S, administered to a subject as part of a pharmaceutical composition, would undergo the formation of cyclic imide to provide thalidomide.

In response, the Examiner concludes, seemingly based on his personal knowledge, that the compounds Q, P, R would under go cyclization to form thalidomide. Apart from the fact that such conclusion is unsupported by any evidence, and that Applicant

expressly disagrees with the Examiner's conclusion, the Examiner provides nothing with regard to the temperature requirement of the alleged "internal cyclization reaction." *See* Applicant's Response of February 22, 2005, page 25. Furthermore, and more importantly, the Examiner does not provide any evidence that the claimed compounds will undergo cyclization to form thalidomide once administered into a patient. Consequently, Applicant respectfully points out that the rejection of the claims, to the extent that it is based on a speculative proposition, cannot be sustained.

For at least the foregoing reasons, Applicant respectfully submits that the pending claims are not obvious, and thus, requests that the rejection of the claims under 35 U.S.C. § 103 be withdrawn.

D. Obviousness-Type Double Patenting

In the Office Action, the provisional rejection of the pending claims under judicially-created obviousness-type double patenting over certain claims of U.S. patent application nos. 09/480,448 and 10/430,892 is maintained. Since these rejections are provisional, Applicant respectfully requests that the rejections be held in abeyance until the claims are found otherwise allowable. Applicant will file a terminal disclaimer, if necessary, at such time.

No fee is believed due for the submission of this paper. If any fees are due for the submission of this paper, or to avoid abandonment of this application, please charge such fees to Jones Day Deposit Account No. 503013. A copy of this sheet is enclosed.

Respectfully Submitted,

Date: September 29, 2005

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